UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO.
09/846,430	04/30/2001	Jennifer H. Lai	5100-7001.0016-US	4378

23419 7590 07/01/2003

COOLEY GODWARD, LLP
3000 EL CAMINO REAL
5 PALO ALTO SQUARE
PALO ALTO, CA 94306

EXAMINER	
SIEW, JEFFREY	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/846,430	LAI ET AL.
	Examiner	Art Unit
	Jeffrey Siew	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1 136(a) In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U S C § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment See 37 CFR 1 704(b)

Status

1)[·] Responsive to communication(s) filed on *12 May 2003* .

2a)[·] This action is **FINAL**. 2b)[ ] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)[·] Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)[ ] Claim(s) _____ is/are allowed.

6)[·] Claim(s) *1-85* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)[ ] The specification is objected to by the Examiner.

10)[·] The drawing(s) filed on _____ is/are: a)[ ] accepted or b)[ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)[ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[ ] All b)[ ] Some * c)[ ] None of:

1.[ ] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No. _____ .

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)[x] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) [ ] Interview Summary (PTO-413) Paper No(s). _____ .
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other: .

DETAILED ACTION

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-85 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,274,323 (August 14, 2001) in view of Balch (US 6,083,763 July 4, 2000).

Claims 1-85 of the instant application are drawn to methods and compositions of detecting an amplification product of a target polynucleotide comprising a first label and capture sequence not in target polynucleotide with further limitations wherein the label is semiconductor nanocrystals.

Claims 1-40 of US 6,274,323 are drawn to detecting amplification product with a binding molecule and semiconductor nanocrystals

Claims 1-40 of US 6,274,323 are not drawn to where the binding molecule is a capture sequence that binds to a capture probe.

Balch teach a method of multiplexed molecular analysis involving providing an amplification product of a polynucleotide comprising a first label and capture sequence, providing a substrate that is conjugated to a first capture probe, contacting sample with capture probe and determining first label is associated with substrate. (see whole doc. col. 35 lines 45-65). Capture probe is a polynucleotide (see col. 17 lines 27-65). They teach glass slides and different wells with glass slides in microplate (see col. 8 line 40, col. 31 lines 31). They teach that the primers have unique universal sequences and complementary to different loci on the template accomplished. (see col. 34 line 43-45). They teach labels such as fluorescein (see col. 34 line 52, col. 32 line 43-45). They teach extension of primer to form amplification product by polymerase (see col. 35 line 43).

One of ordinary skill in the art would have been motivated to apply Balch et al's teaching of capture sequence in primer in order specifically capture amplified target nucleic acids. Balch teach that the use of different capture sequences allows multiple detection of different targets simultaneously on a single assay. It would have been prima facie obvious to apply Balch et al's different capture sequences in order to detect different targets simultaneously.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-5,12-15 ,21-28,38-42, 43- 45, 52,53, 55- 62,68,70,72,74-76 & 80-84 are rejected under 35 U.S.C. 102(e) as being anticipated by Balch (US6,083,763 July 4, 2000).

Balch teach a method of multiplexed molecular analysis involving providing an amplification product of a polynucleotide comprising a first label and capture sequence, providing a substrate that is conjugated to a first capture probe, contacting sample with capture probe and determining first label is associated with substrate. (see whole doc. col. 35 lines 45-65). Capture probe is a polynucleotide (see col. 17 lines 27-65). They teach glass slides and different wells with glass slides in microplate (see col. 8 line 40, col. 31 lines 31). They teach that the primers have unique universal sequences and complementary to different loci on the template accomplished. (see col. 34 line 43-45). They teach labels such as fluorescein (see col. 34 line 52, col. 32 line 43-45). They teach extension of primer to form amplification product by polymerase (see col. 35 line 43). They teach alkaline phosphatase (see col. 25 line 15). They teach dioxigenin or biotin (see col. 25 line 9). They teach lathanide (LN) chelators (see col. 26

lines 36). They teaching using multiple different labels to different biosites (see col. 32 line 43-46 & fig. 19D). They teach mRNA analytes, DNA , RNA analytes (see col. 8 lines 18-20). They teach testing for plurality of targets including three and four loci and 25 different loci (see figures 14, 15 & 17). They teach detecting SNP (see col. 34 line 19). They teach use of exonuclease to digest non extended primers (see col.34 line 47). Attachment of capture probes may be by 3' or 5' end thru carboxylated derivative (see col. 18 lines 55-67).

3. The response filed 5/12/03 has been fully considered and deemed not persuasive. The response states that Balch et al do not teach the amplification product that is made by primer extension product which is bifunctional oligonucleotide containing a target complementary region and target noncomplementary region and from template then formed the second PEP is formed with labeled primer. Balch et al do teach the PEP (see Figure 15) with 12m er universal handle primer for binding support that is not complementary to target and primer region that is compelementary to target and corresponding fluroescently labeled primer that binds to template to form the amplification product. The rejection is maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-11,16-20,29-37,46-51,54,63-65,69,71, 73,77 & 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balch (US6,083,763 July 4, 2000) in view of Bruchez et al (US 6,274,323 August 14, 2001).

The teachings of Balch are described previously.

Balch do not teach semiconductor nanocrystals, detecting alleles, primer is within five nucleotides of first primer.

Bruchez et al teach using semiconductor nanocrystals in microspheres as detectable labels with different wavelengths (see whole doc. esp. abstract). They shell and core with CdSe (see col. 9 lines 1-62). They also teach the use of aptamers. The teach detection using allele specific primer (see col. 52 line 6). They teach RT –PCR (see claim 23).They also teach the SNPs within five nucleotides within 3` end (see col. 50 lines 60-65).

One of ordinary skill in the art would have been motivated to apply Bruchez et al`s teachings in particular semiconductor nanocrystals in order to provide higher fluorescent intensity and high stability. Bruchez teach that nanocrystals provide high fluorescent intensity, adequate separation between absorption and emission frequencies, readily linkable, and high

stability (see col. 4 lines 30-37). It would have been prima facie obvious to apply Bruchez et al's nanocrystals in order to increase the detection of labeled targets.

Moreover one of ordinary skill in the art would have been motivated to apply Bruchez teachings of allele primers and SNP primers to Balch's PCR detection method in order to detect mutations. It would have been prima facie obvious to apply Bruchez allele primers and SNP primers in order to genotype individuals for disease related mutations.

5. Claims 6-10,16-20,30-37,46,48-51,69,71, 73,77 & 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balch (US6,083,763 July 4, 2000) in view of Weiss (US6,207,392 B1 March 27,2001)

The teachings of Balch are described previously.

Balch do not teach semiconductor nanocrystals.

Weiss et al teach using semiconductor nanocrystals in microspheres as detectable labels with different wavelengths (see whole doc. esp. abstract). They shell and core with CdSe (see col. 7 lines 35-65).

One of ordinary skill in the art would have been motivated to apply Bruchez et al's teachings in particular semiconductor nanocrystals in order to provide higher fluorescent intensity and high stability. Weiss teach that nanocrystals provide for increased number of different dye molecules that may be utilized simultaneously (see col. 1 lines 45-50). It would have been prima facie obvious to apply Bruchez et al's nanocrystals in order to detect different targets simultaneously.

6. Claims 29,47,54,63-65,78 &79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balch (US6,083,763 July 4, 2000) in view of Duckworth et al (US 6,426,197 July 30, 2002).

The teachings of Balch are described previously.

Balch do not teach detecting alleles, primer is within five nucleotides of first primer.

Duckworth et al teach detection using allele specific primer (see col. 14 line 50-65 line 6). They teach RT –PCR (see col. 8 line 25).They also teach the SNP base at 3` end (see col. 14 lines 61).

One of ordinary skill in the art would have been motivated to apply Duckworth et al`s teachings of allele primers and SNP primers to Balch`s PCR detection method in order to detect mutations. It would have been prima facie obvious to apply Bruchez allele primers and SNP primers in order to genotype individuals for disease related mutations.

7. Claims 66 & 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balch (US6,083,763 July 4, 2000) in view of Duckworth et al (US 6,726,197 July 20, 2002) in further view of Ellis et al (US 5,942,394 August 24, 1999).

The teachings of Balch are described previously.

Balch do not teach flanking primers

Ellis teach flanking primers with lower melting point (see col. 3 line50-60).

One of ordinary skill in the art would have been motivated to apply Ellis et al`s teachings of flanking primers to Balch`s PCR detection method in order to detect mutations. Ellis et al

teach that flanking primers provide for delay on non specific amplification products (see col.3 lines 65-col.4 lines 3). It would have been prima facie obvious to apply Ellis et al's flanking primers in order to avoid non specific amplification product.

8. The response regarding the 103 rejections has been fully considered and deemed not persuasive. First the response states that Bruchez filing date is less than one year prior to effective filing date of present application and would only be citable under 102 e, f and g and cannot be used to preclude patentablility under 103a. MPEP 2146 state sthat subject matter developed by antoher which qualifies as prior art only under one of the following 102 e,f and g is not to be considered under obviousness under 103. However, Bruchez prior art would be based on 102 a date which would still provide the basis for 103 a rejection. The response then cites much case law detailing the obviousness standards and repeats the basis of the 102 argument that Balch do not teach the amplification product with label and capture sequence. As stated previously, Balch et al do teach the PEP (see Figure 15) with 12m er universal handle primer for binding support that is not complementary to target and primer region that is compelementary to target and corresponding fluroescently labeled primer that binds to template to form the amplification product.

SUMMARY

9. No claims allowed.

Conclusion

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Tracey Johnson for Art Unit 1637 whose telephone number is (703)-305-2982.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Before Final FAX (703) 872-9306 or After Final FAX (703) 30872-9307.

JEFFREY SIEW
PRIMARY EXAMINER

June 29, 2003